Supplementary Material

A biomimetic domino reaction for the concise synthesis of capreomycidine and epicapreomycidine

Martin Büschleb,[‡] Markus Granitzka,[†] Dietmar Stalke,[†] Christian Ducho[‡§*]

[‡]*Georg-August-University Göttingen, Department of Chemistry, Institute of Organic and Biomolecular Chemistry, Tammannstr. 2, 37 077 Göttingen, Germany*

[†]*Georg-August-University Göttingen, Department of Chemistry, Institute of Inorganic Chemistry, Tammannstr. 4, 37 077 Göttingen, Germany*

[§]*University of Paderborn, Department of Chemistry, Warburger Str. 100, 33 098 Paderborn, Germany*

*Corresponding author *E-mail: christian.ducho@uni-paderborn.de*

Table of contents

NMR-based determination of the configuration of δ-azido-didehydro α-amino acids 11a and 21

Mazurkiewicz et al. have established the following ^{1}H NMR criteria (CDCl$_3$) for the distinction of (Z)- and (E)-acyl didehydro amino acids (Mazurkiewicz R, Kuźnik A, Grymel M, Kuźnik N (2005) ^{1}H NMR spectroscopic criteria for the configuration of N-acyl-α,β-dehydro-α-amino acid esters. Magn. Reson. Chem. 43:36-40):

δ^{H-3} (Z) < δ^{H-3} (E) and

δ^{NH} (Z) < δ^{NH} (E)

For **11a** and **21**, the following chemical shifts were observed:

(Z)-**11a**: 6.19 (NH), 6.38 (H-3)   (Z)-**21**: 6.45 (H-3, NH)

(E)-**11a**: 6.66 (H-3), 6.74 (NH)   (E)-**21**: 6.76 (H-3), 6.98 (NH)

These data are in complete agreement with the established criteria and therefore reveal the (Z)-configured didehydro amino acids to be the main products of the respective Wittig-Horner reactions.
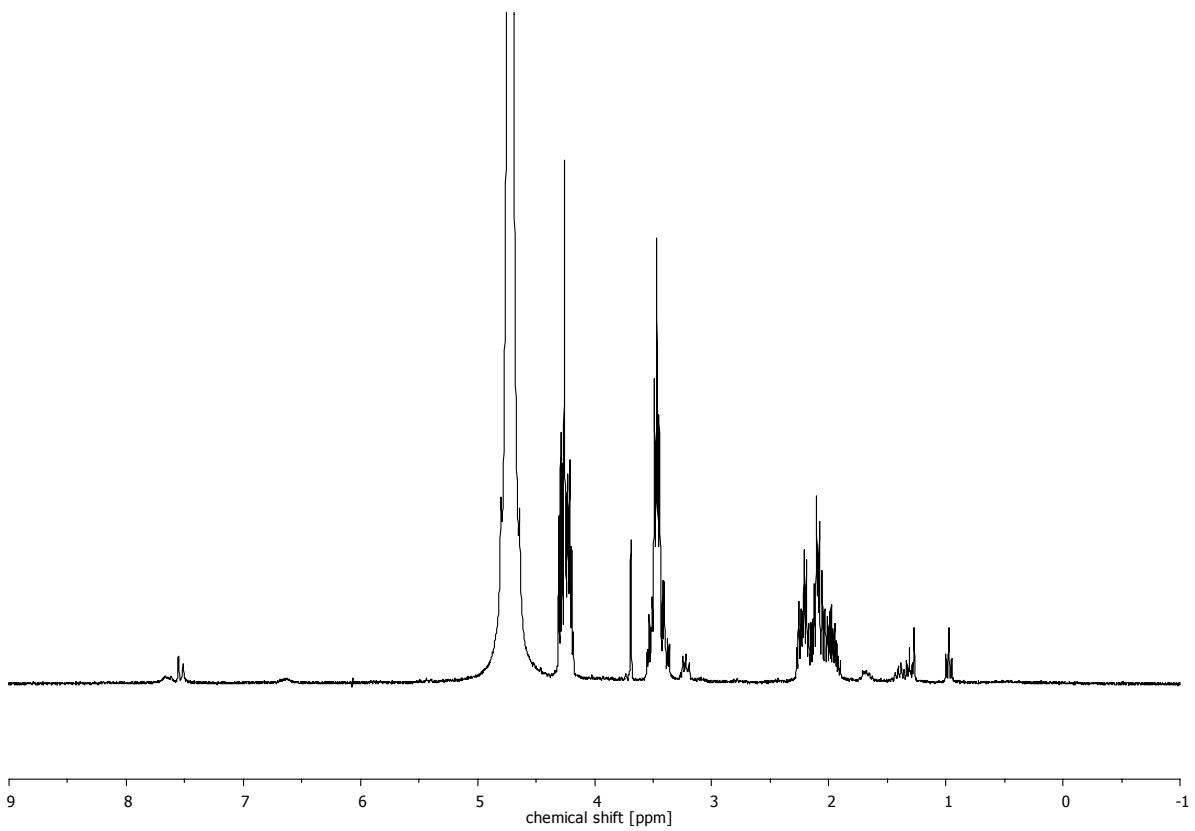
^{1}H NMR spectrum of the mixture of (*rac*)-**1** · 2 HCl and (*rac*)-**2** · 2 HCl (300 MHz, D$_2$O)
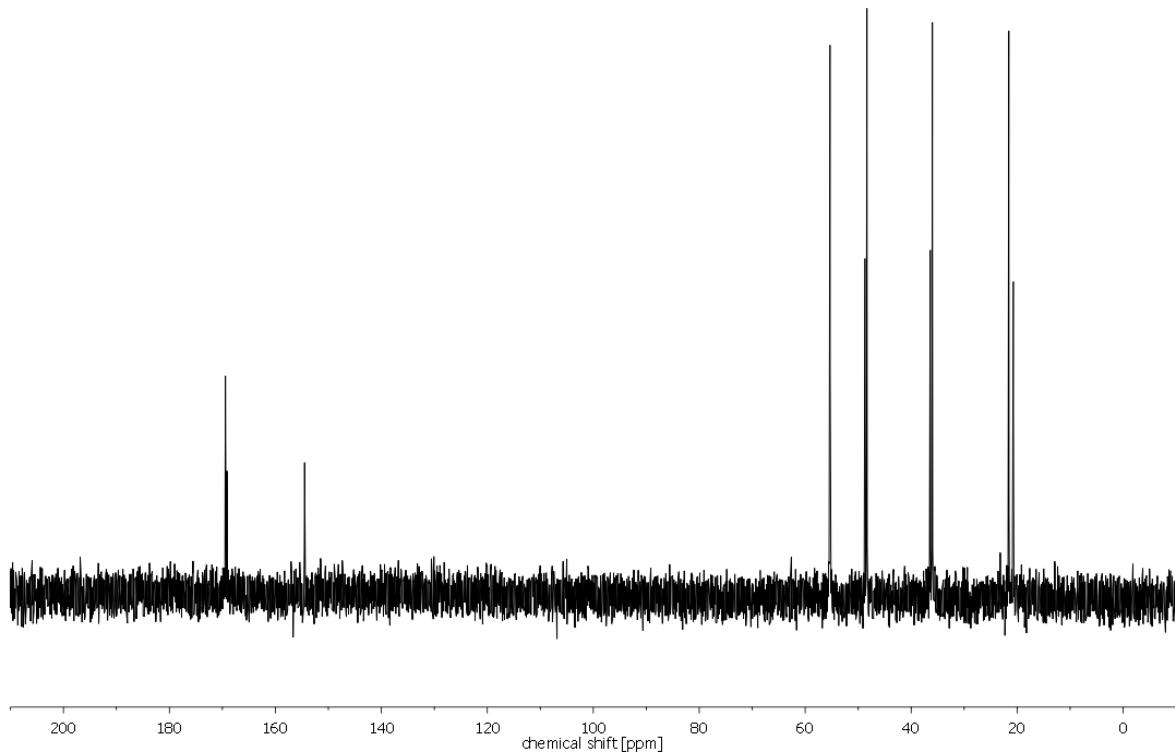
^{13}C NMR spectrum of the mixture of (*rac*)-**1** · 2 HCl and (*rac*)-**2** · 2 HCl (76 MHz, D$_2$O)
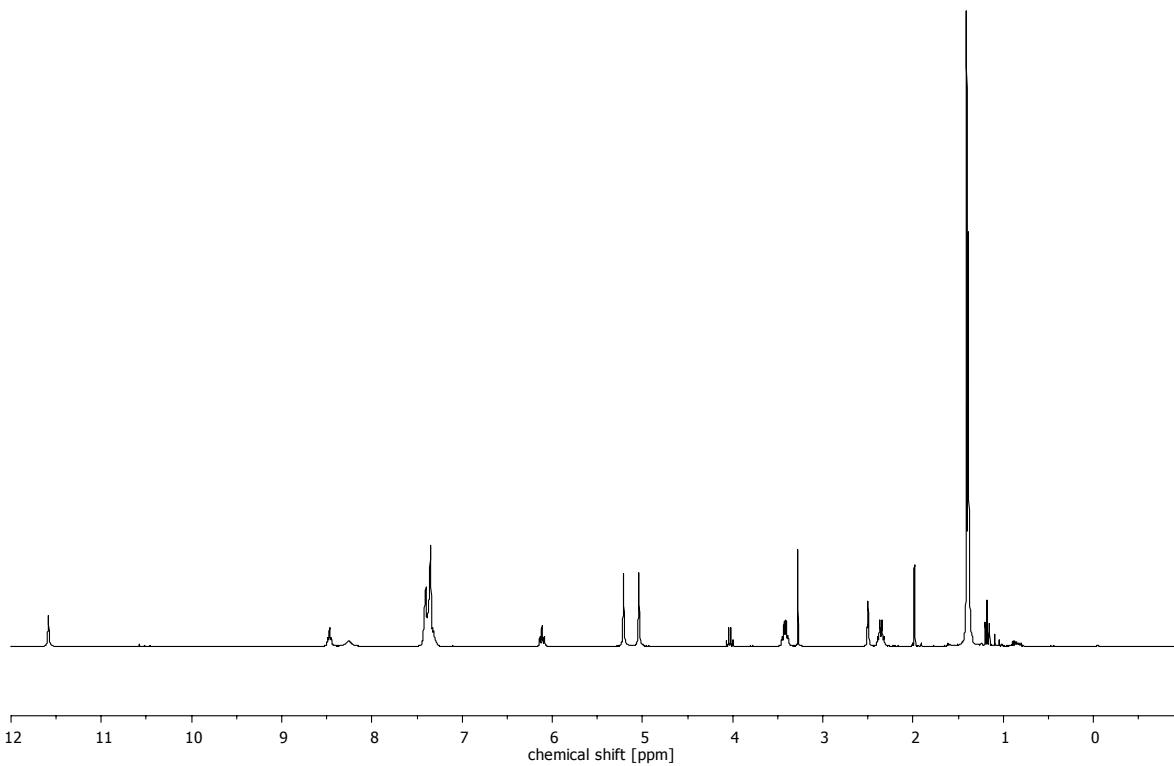
^{1}H NMR spectrum of **8e** (300 MHz, DMSO-d$_6$)
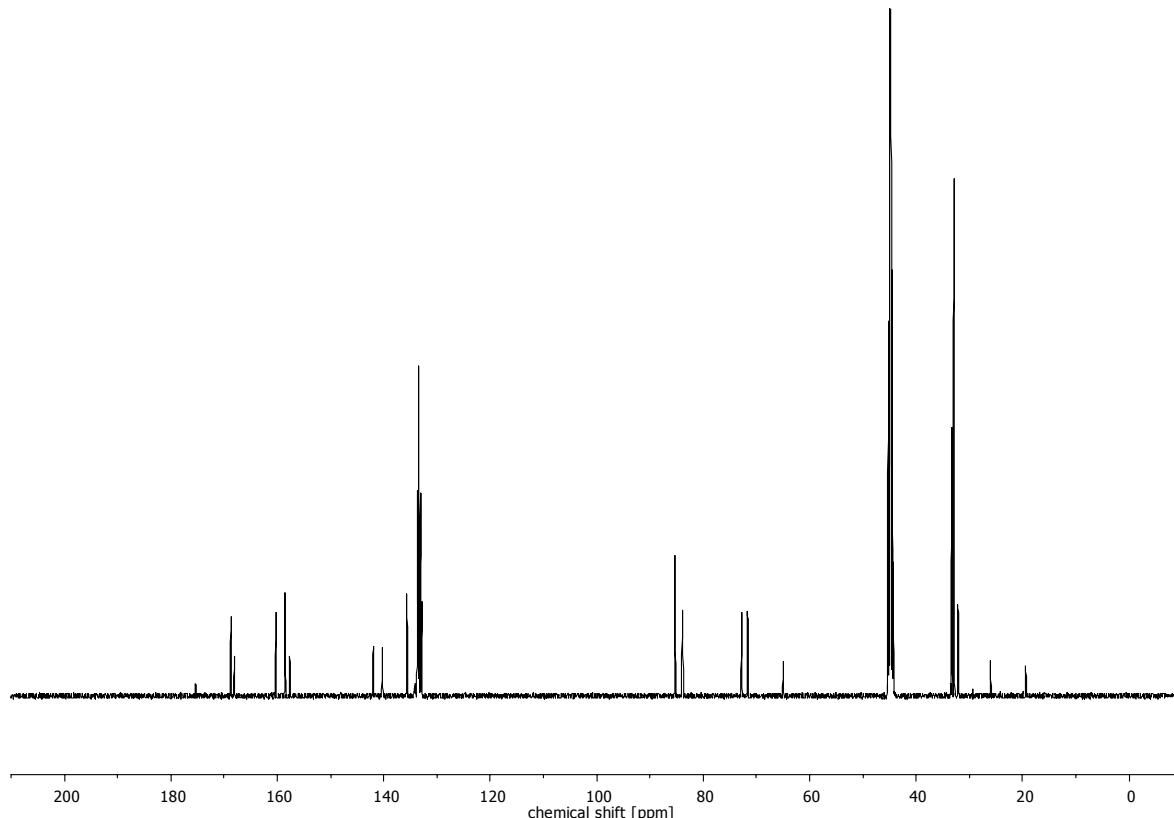
^{13}C NMR spectrum of **8e** (126 MHz, DMSO-d$_6$)
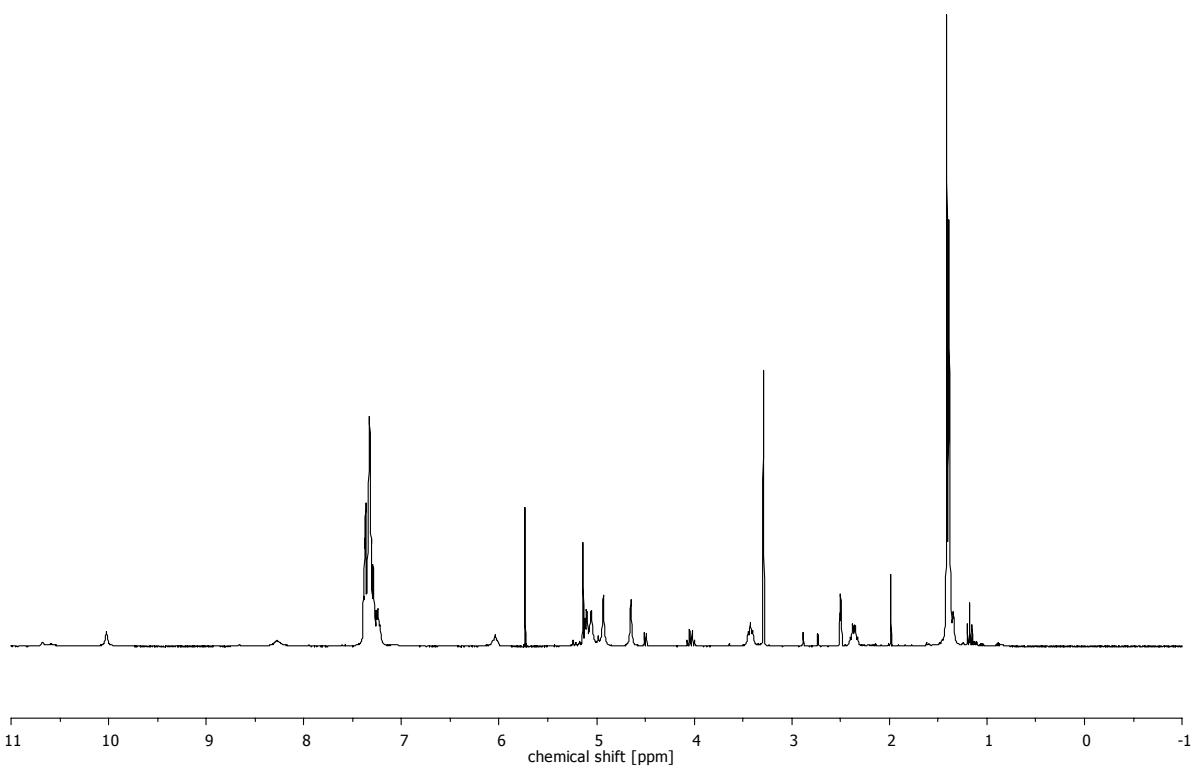
^{1}H NMR spectrum of **8f** (300 MHz, DMSO-d$_6$)
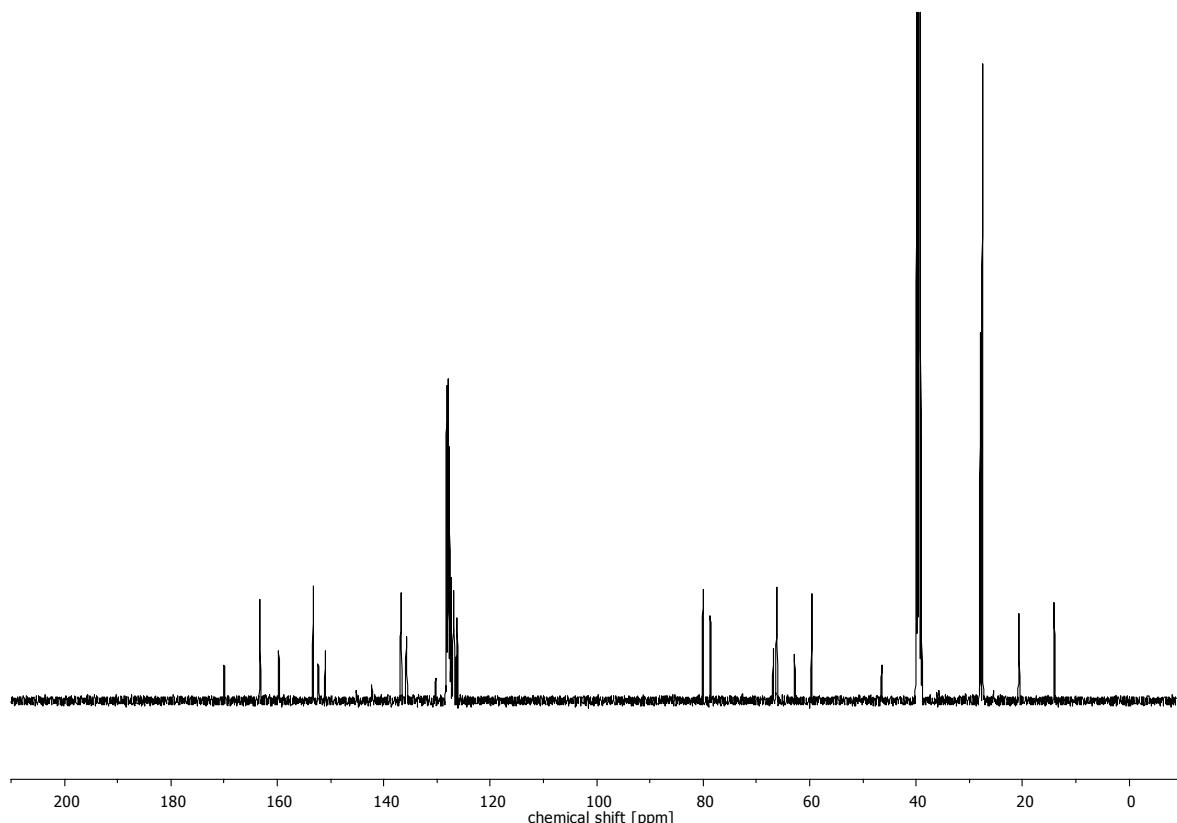
^{13}C NMR spectrum of **8f** (126 MHz, DMSO-d$_6$)
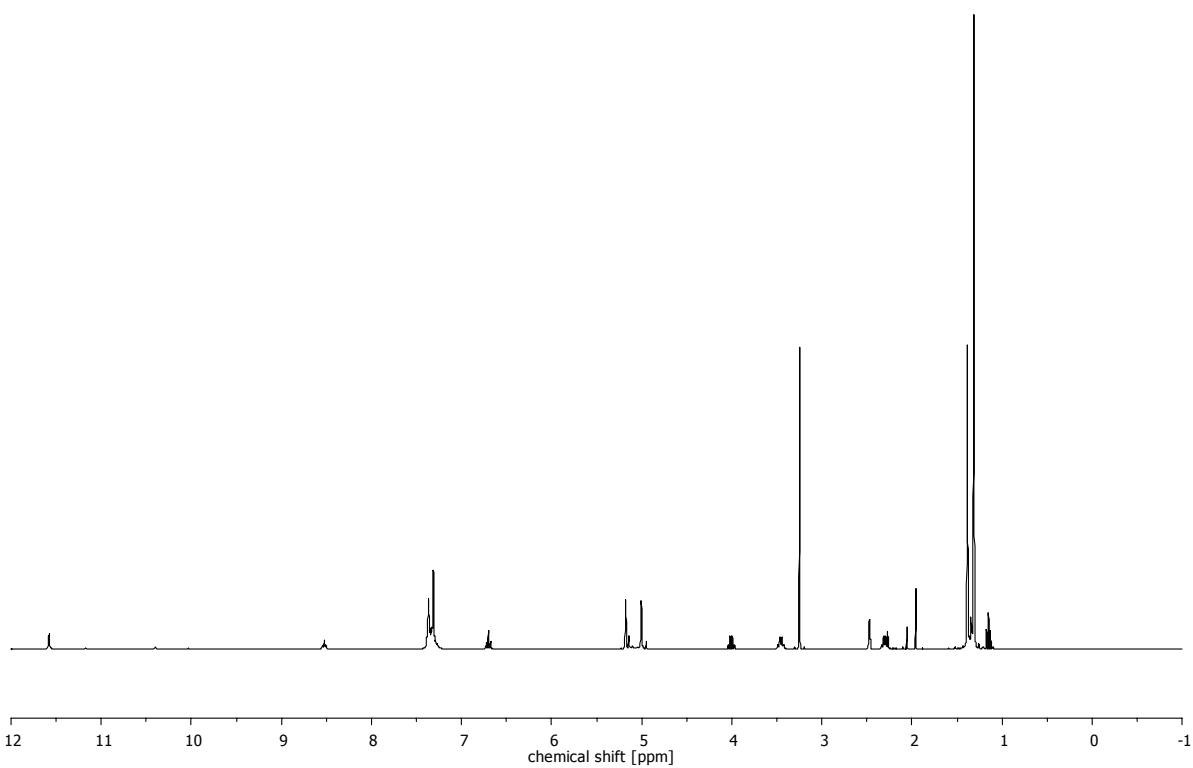
^{1}H NMR spectrum of **8g** (300 MHz, DMSO-d$_6$)
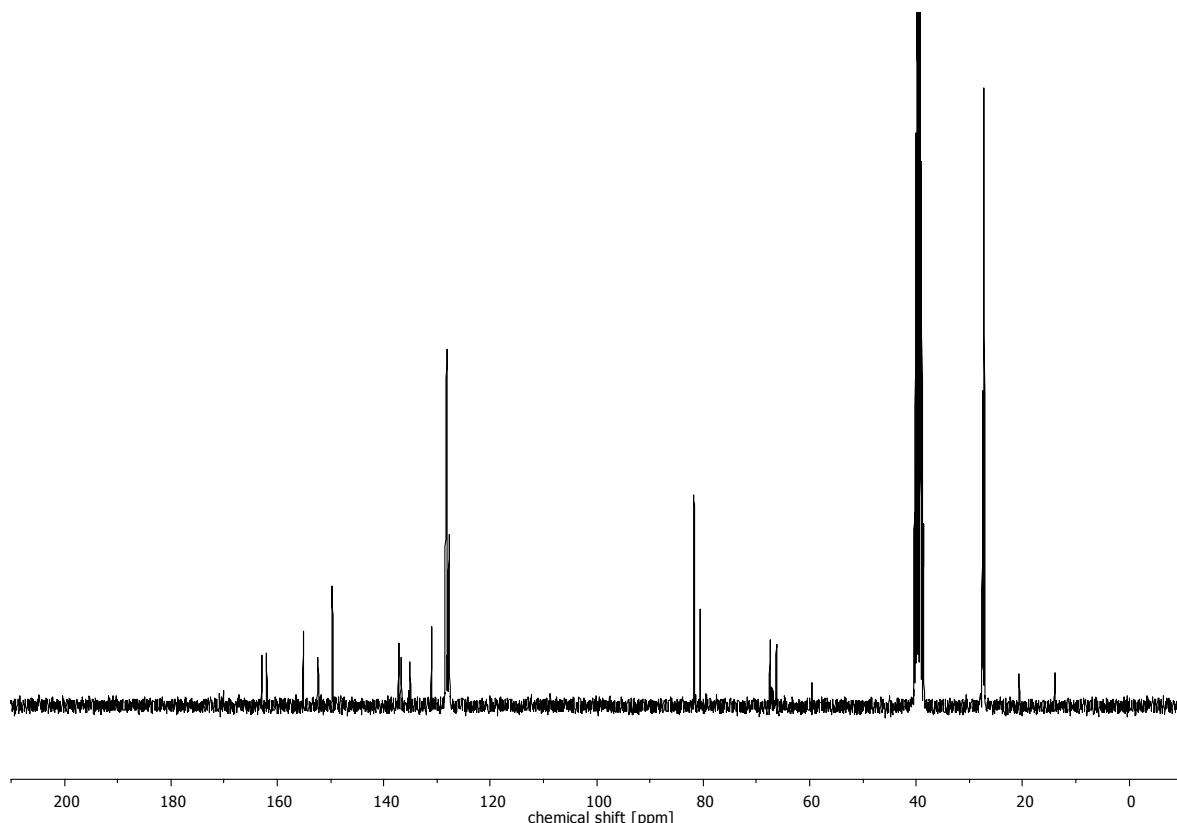
^{13}C NMR spectrum of **8g** (76 MHz, DMSO-d$_6$)
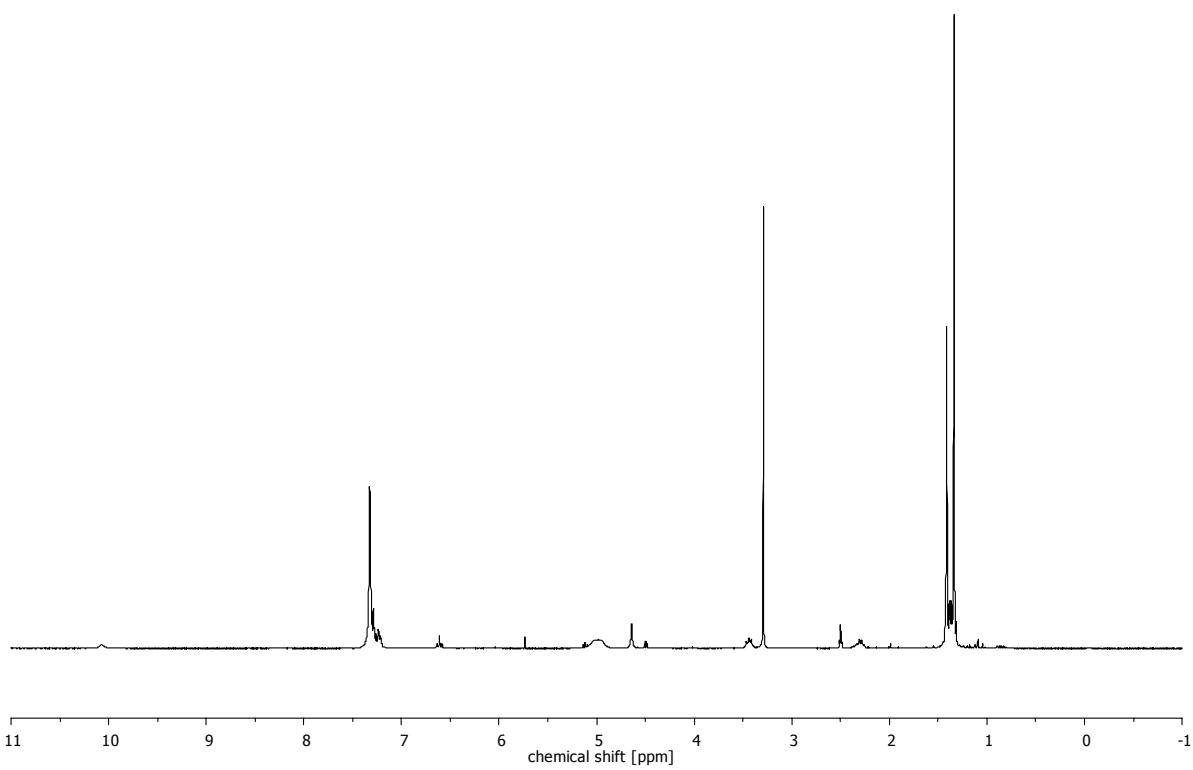
^{1}H NMR spectrum of **8h** (300 MHz, DMSO-d$_6$)
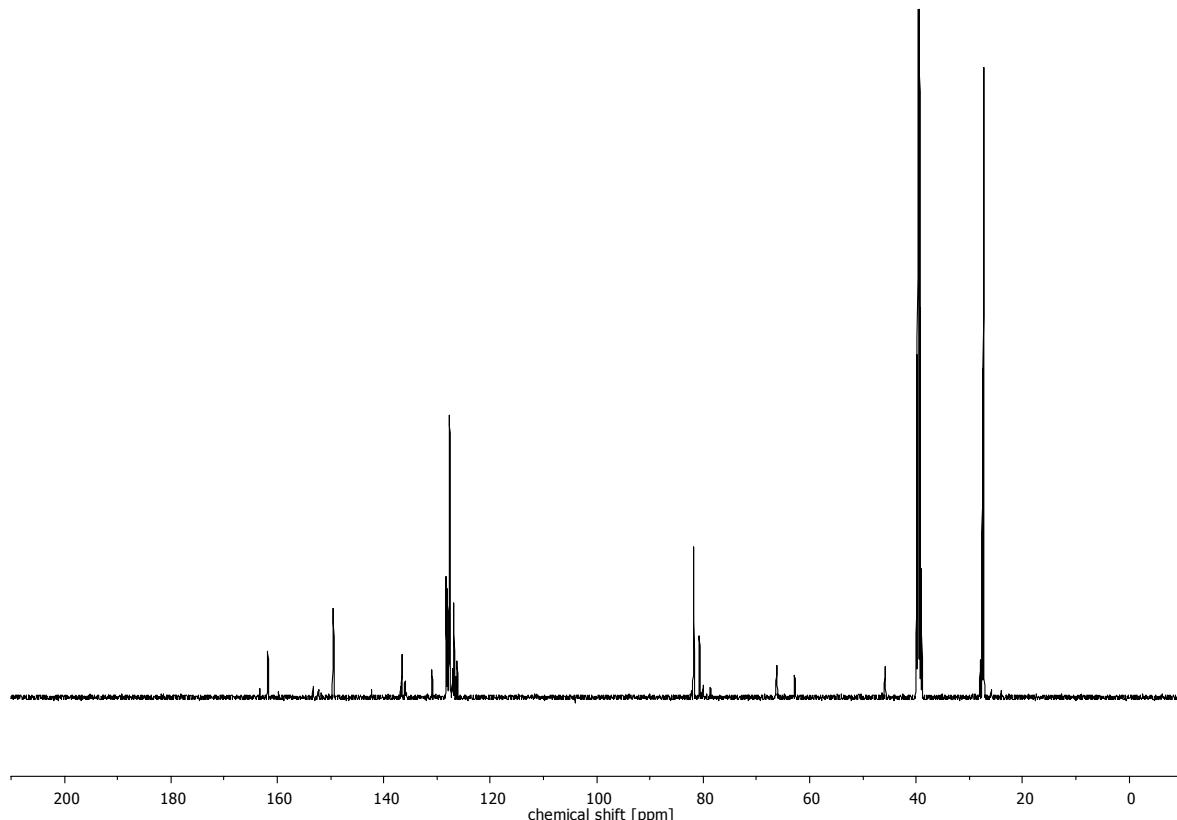
^{13}C NMR spectrum of **8h** (126 MHz, DMSO-d$_6$)
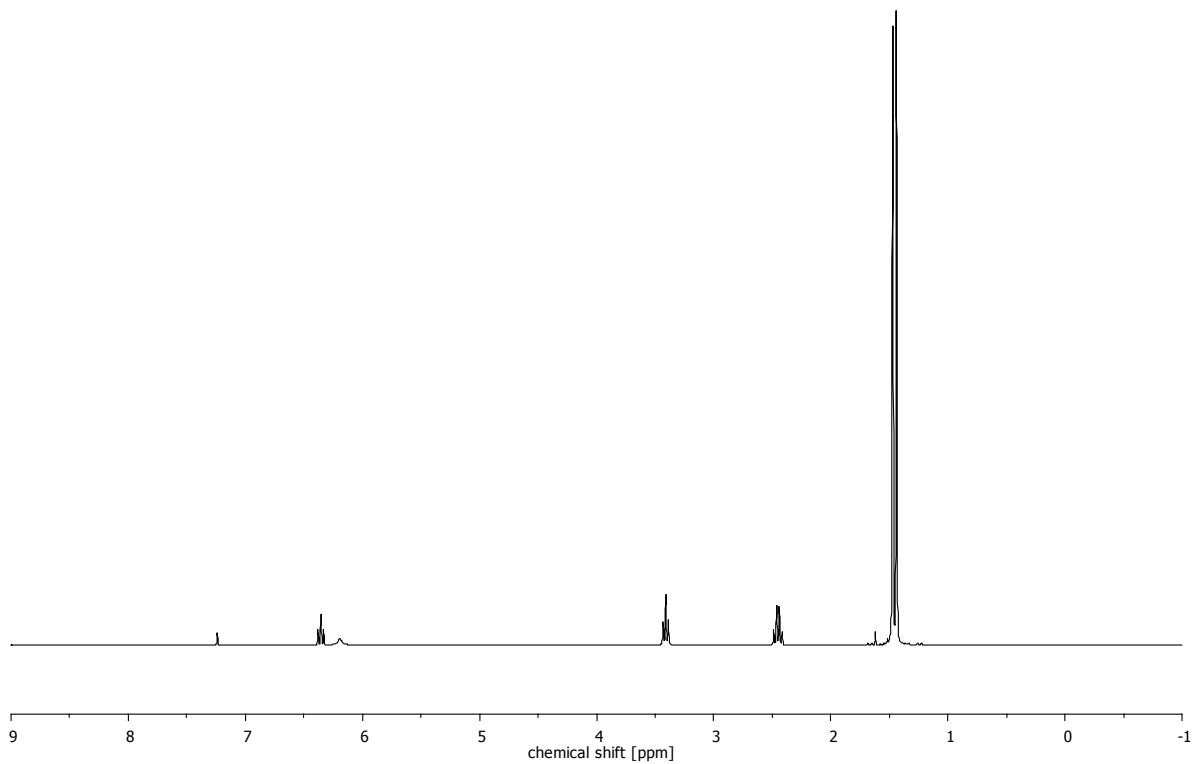
^{1}H NMR spectrum of (*Z*)-**11a** (300 MHz, CDCl$_3$)
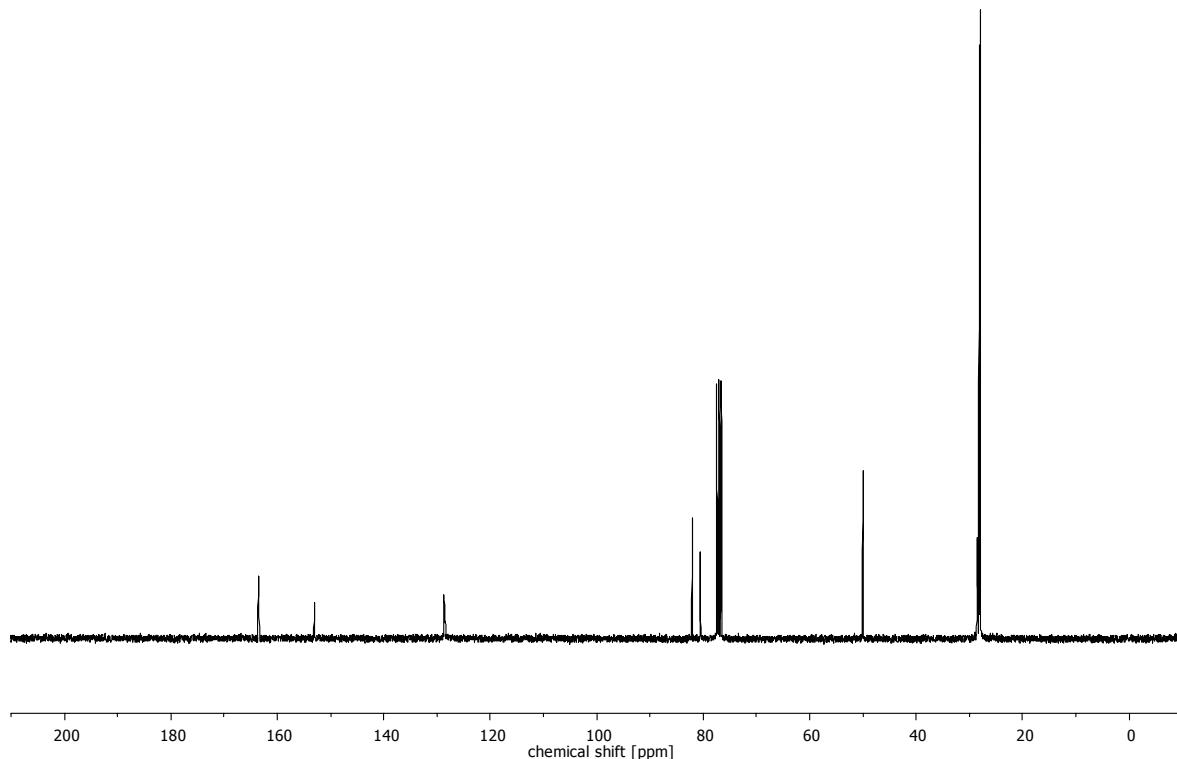

^{13}C NMR spectrum of (*Z*)-**11a** (76 MHz, CDCl$_3$)

S8
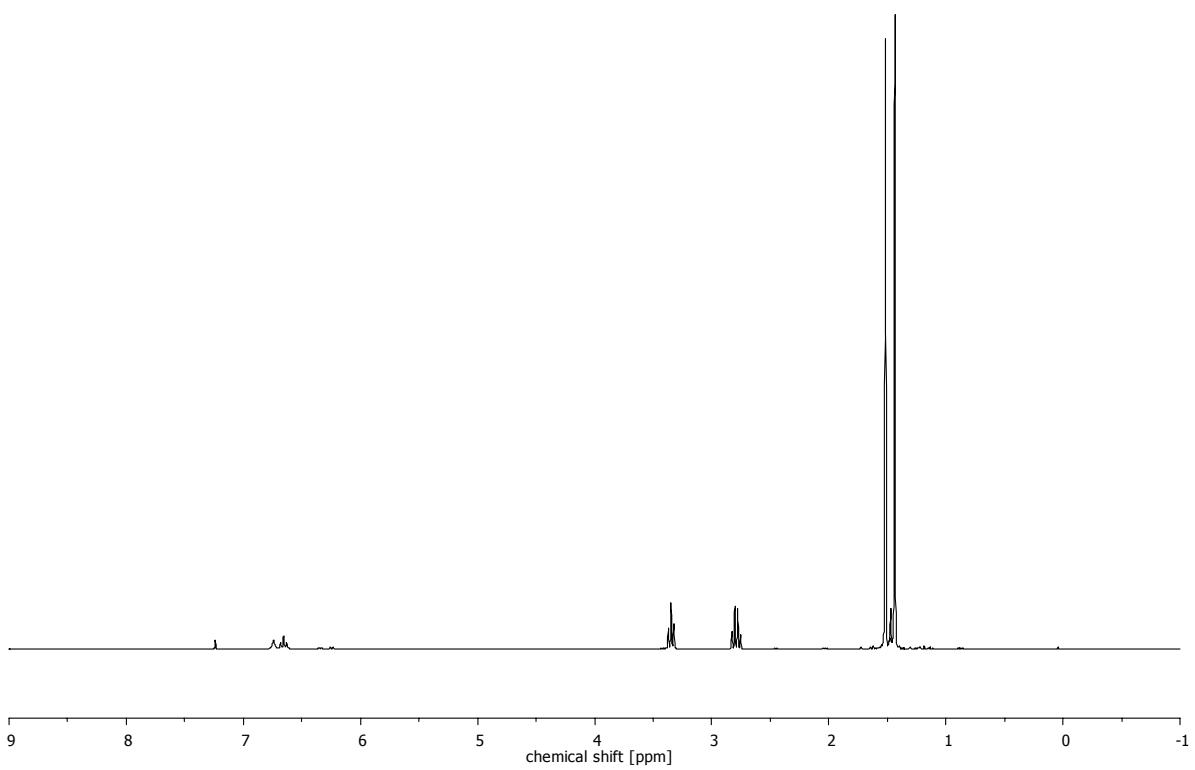
^{1}H NMR spectrum of (*E*)-**11a** (300 MHz, CDCl$_3$)
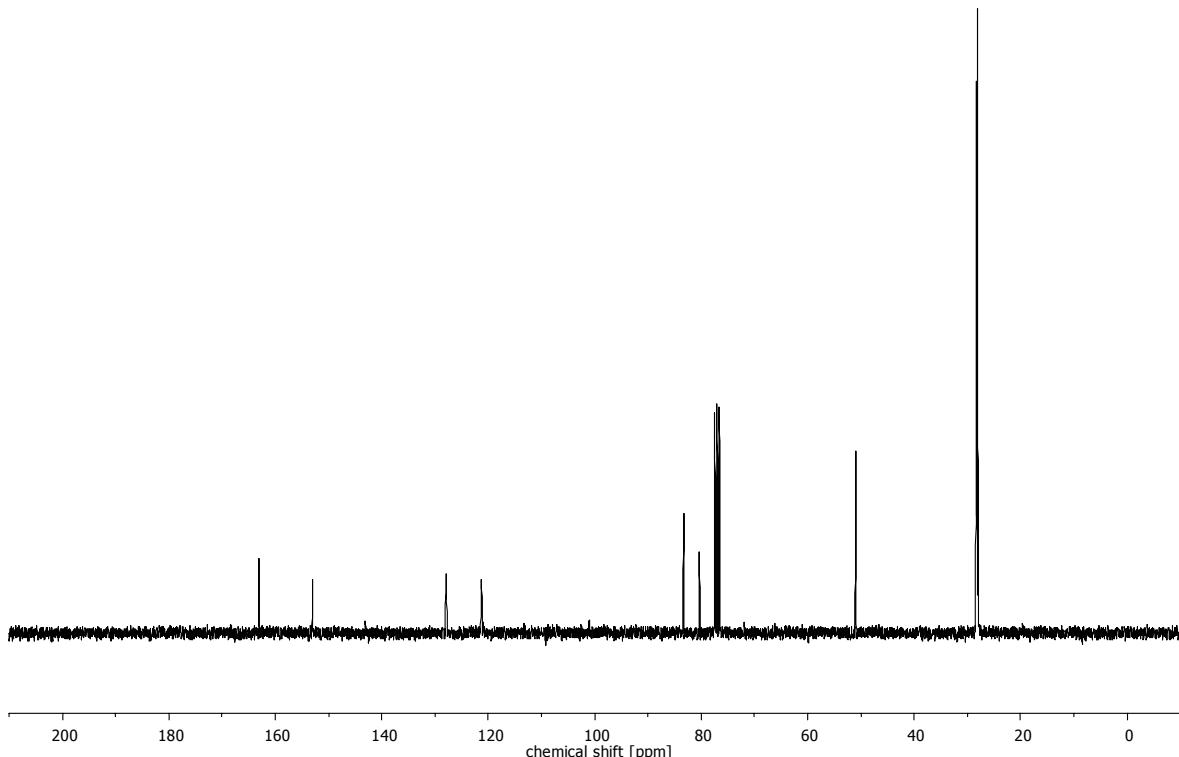
^{13}C NMR spectrum of (*E*)-**11a** (76 MHz, CDCl$_3$)
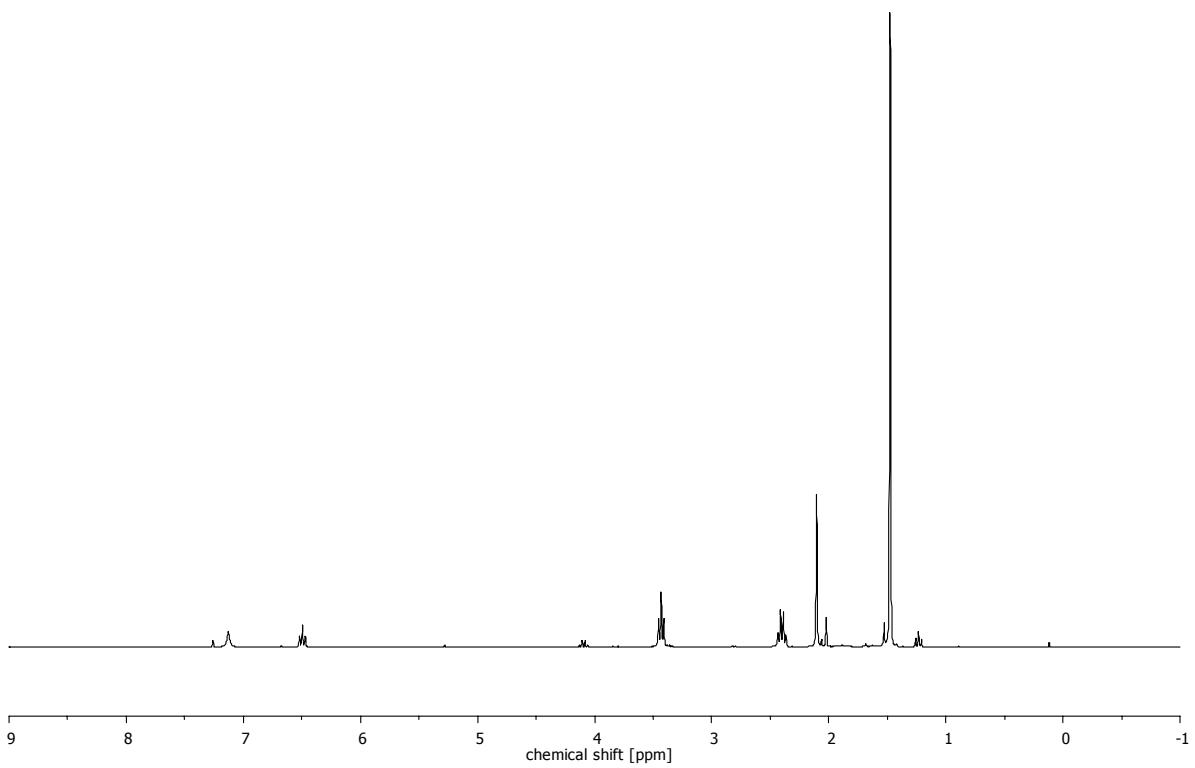
^{1}H NMR spectrum of (*Z*)-**11b** (300 MHz, CDCl$_3$)
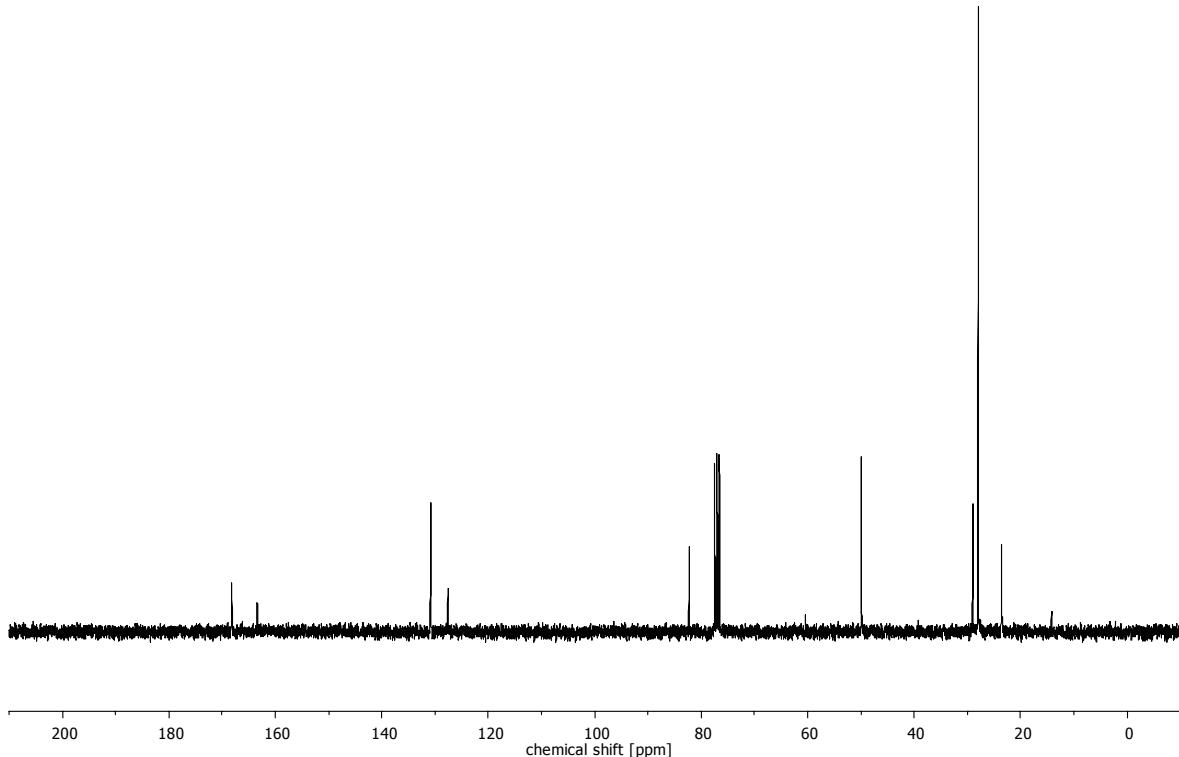
^{13}C NMR spectrum of (*Z*)-**11b** (75 MHz, CDCl$_3$)
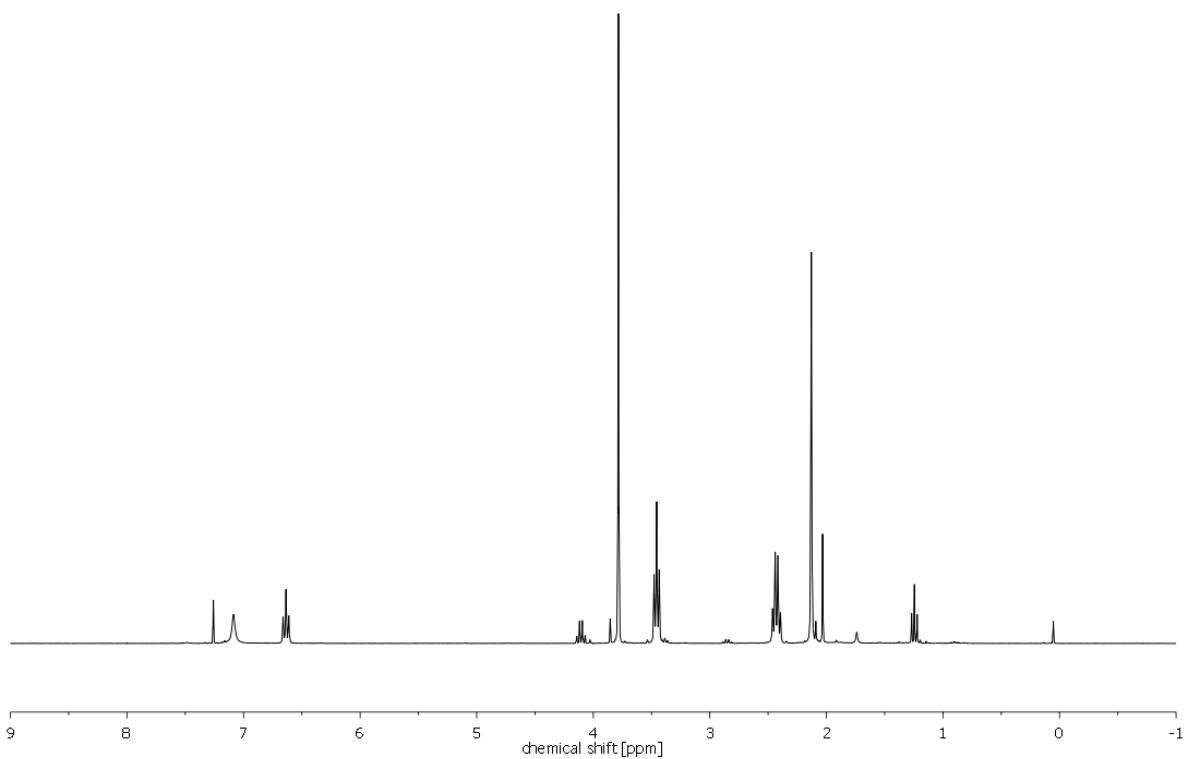
^{1}H NMR spectrum of (*Z*)-**11c** (300 MHz, CDCl$_3$)
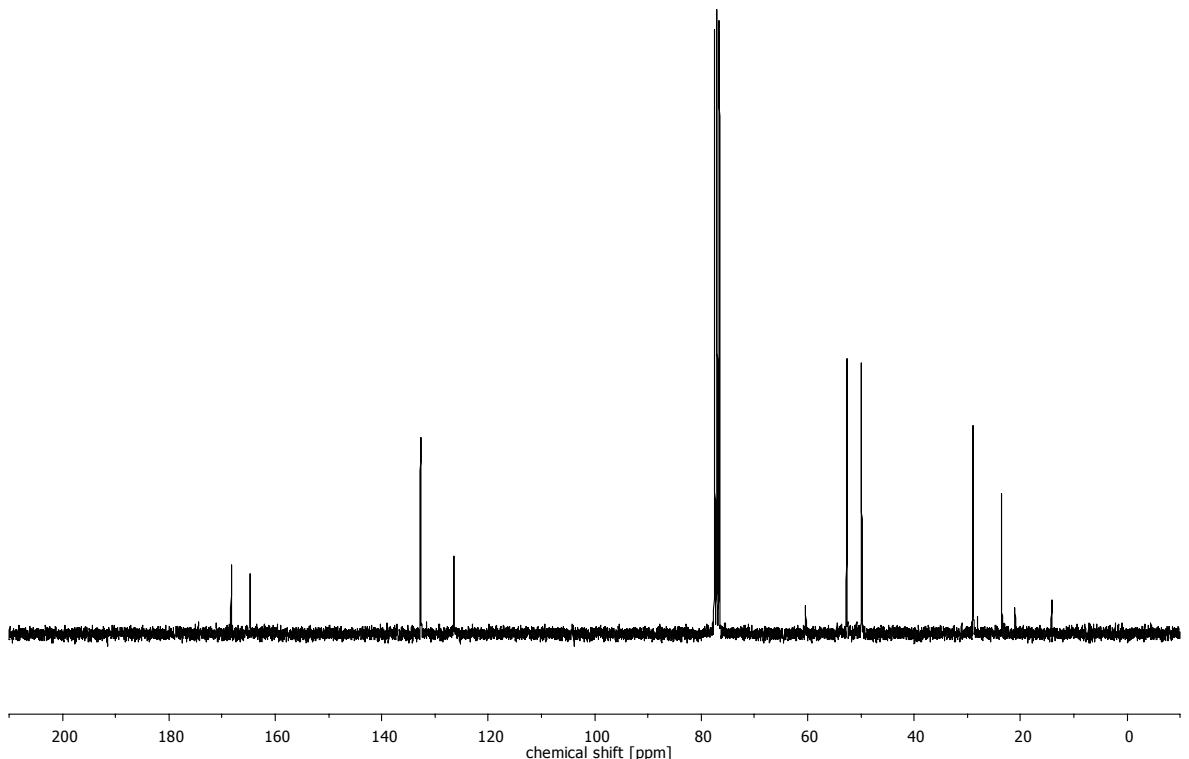
^{13}C NMR spectrum of (*Z*)-**11c** (76 MHz, CDCl$_3$)
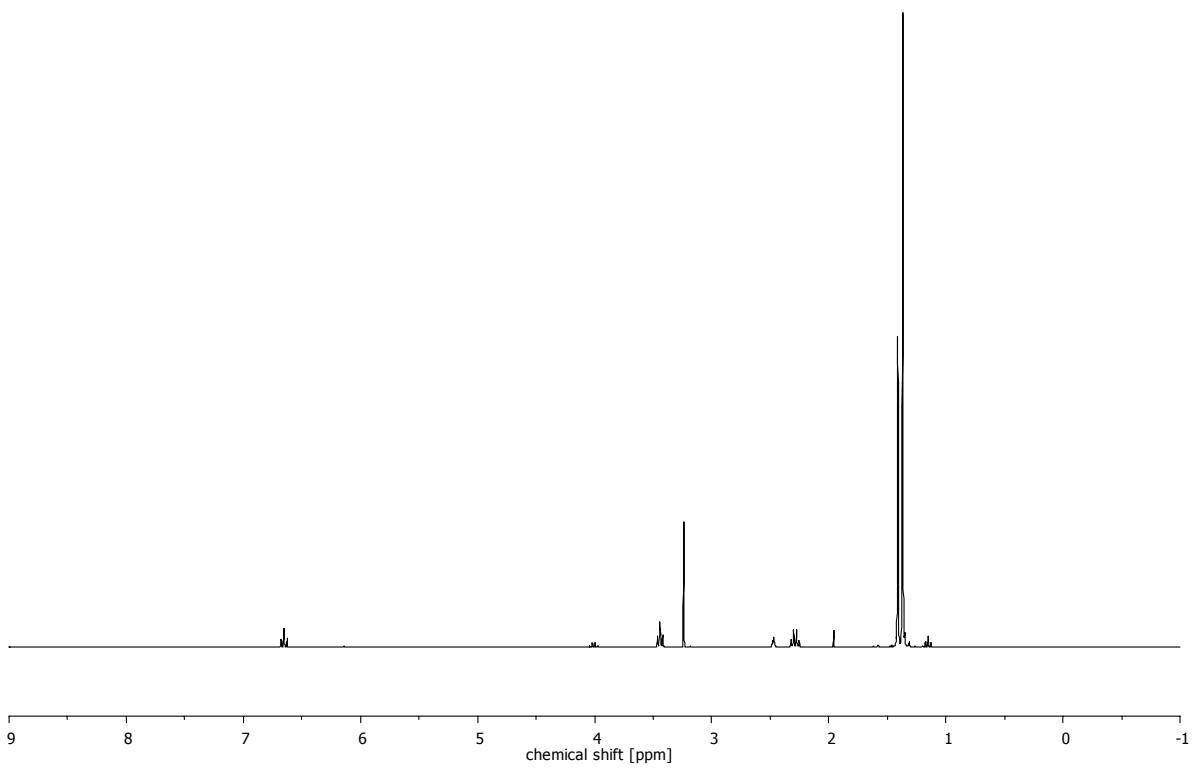
^{1}H NMR spectrum of (*Z*)-**11d** (300 MHz, DMSO-d$_6$)
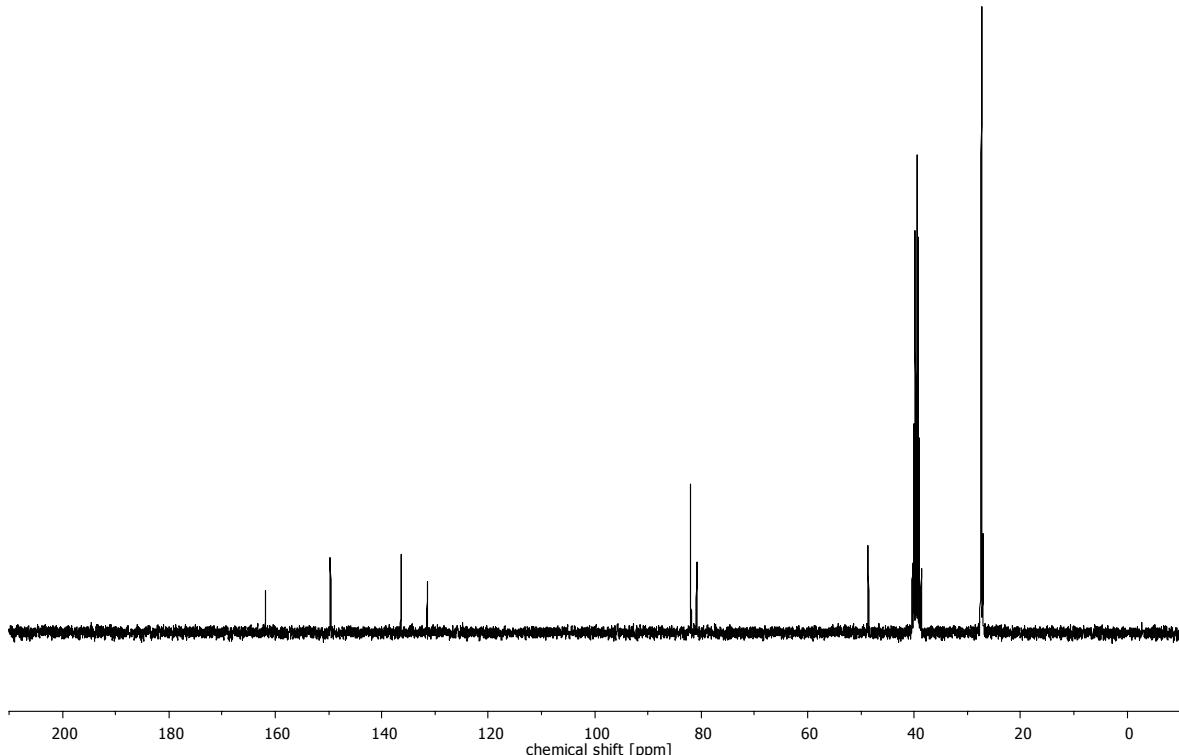
^{13}C NMR spectrum of (*Z*)-**11d** (76 MHz, DMSO-d$_6$)
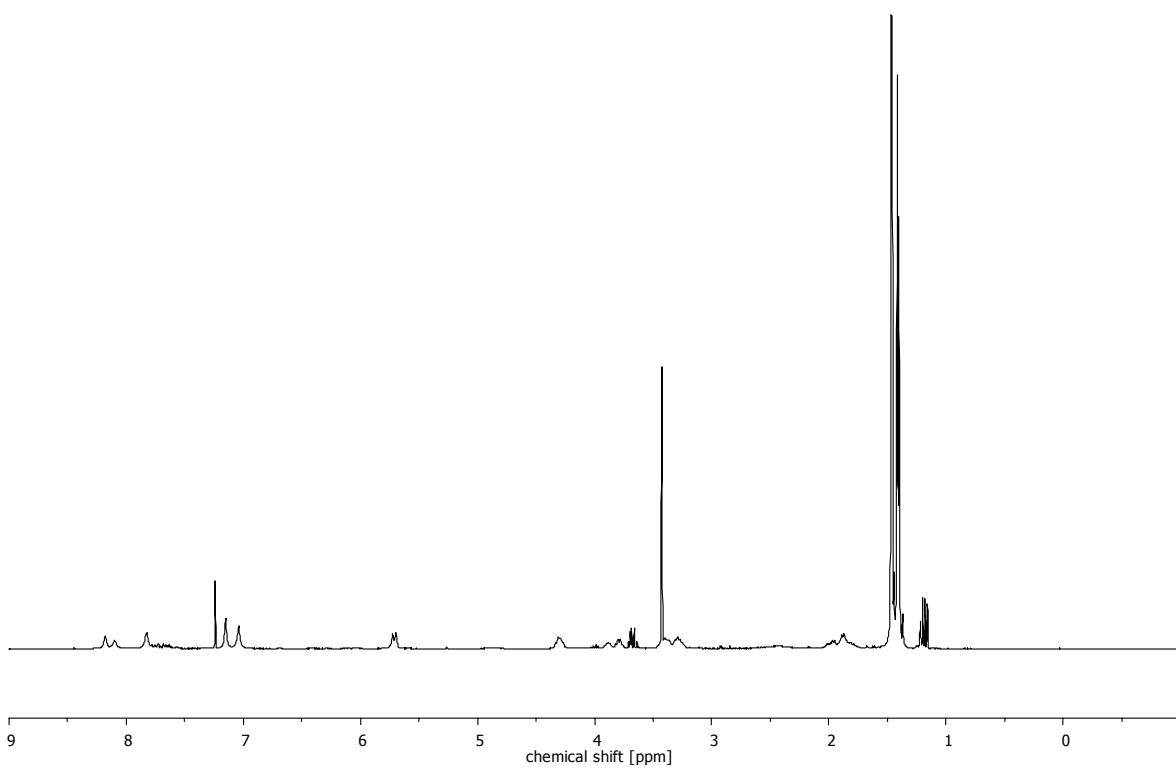
^{1}H NMR spectrum of the mixture of (*rac*)-**14** and (*rac*)-**15** (300 MHz, CDCl$_3$)
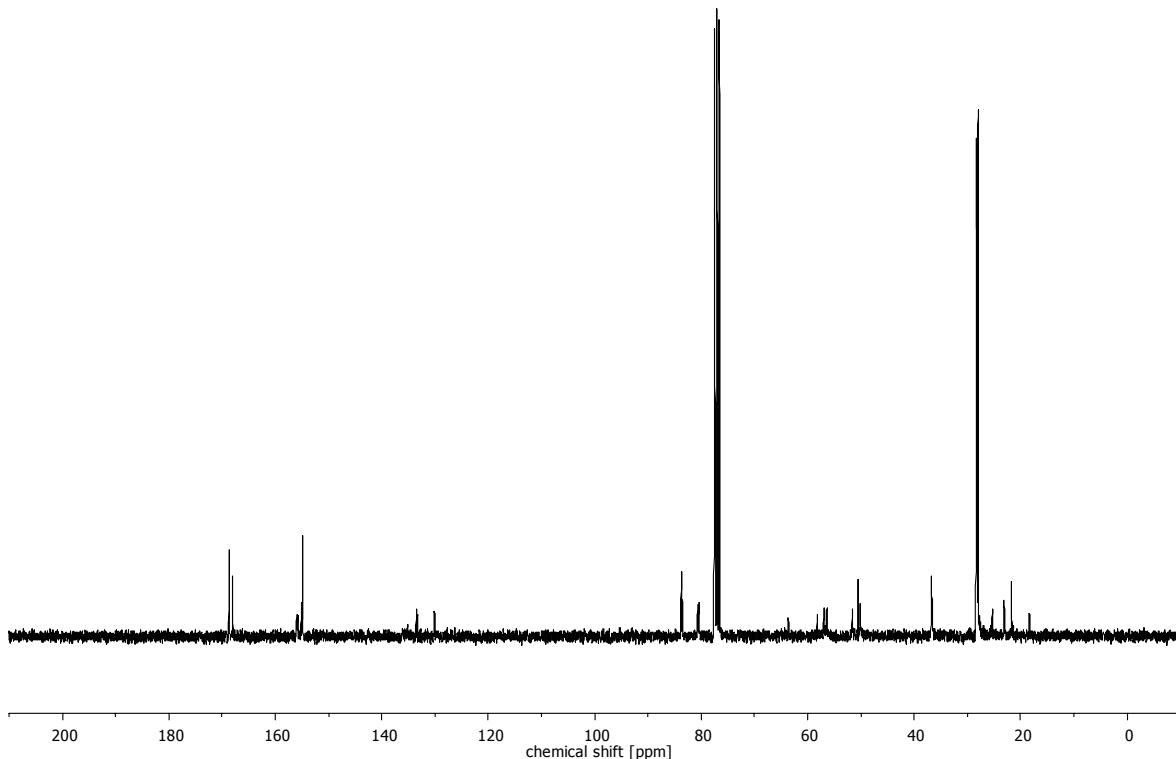
^{13}C NMR spectrum of the mixture of (*rac*)-**14** and (*rac*)-**15** (76 MHz, CDCl$_3$)
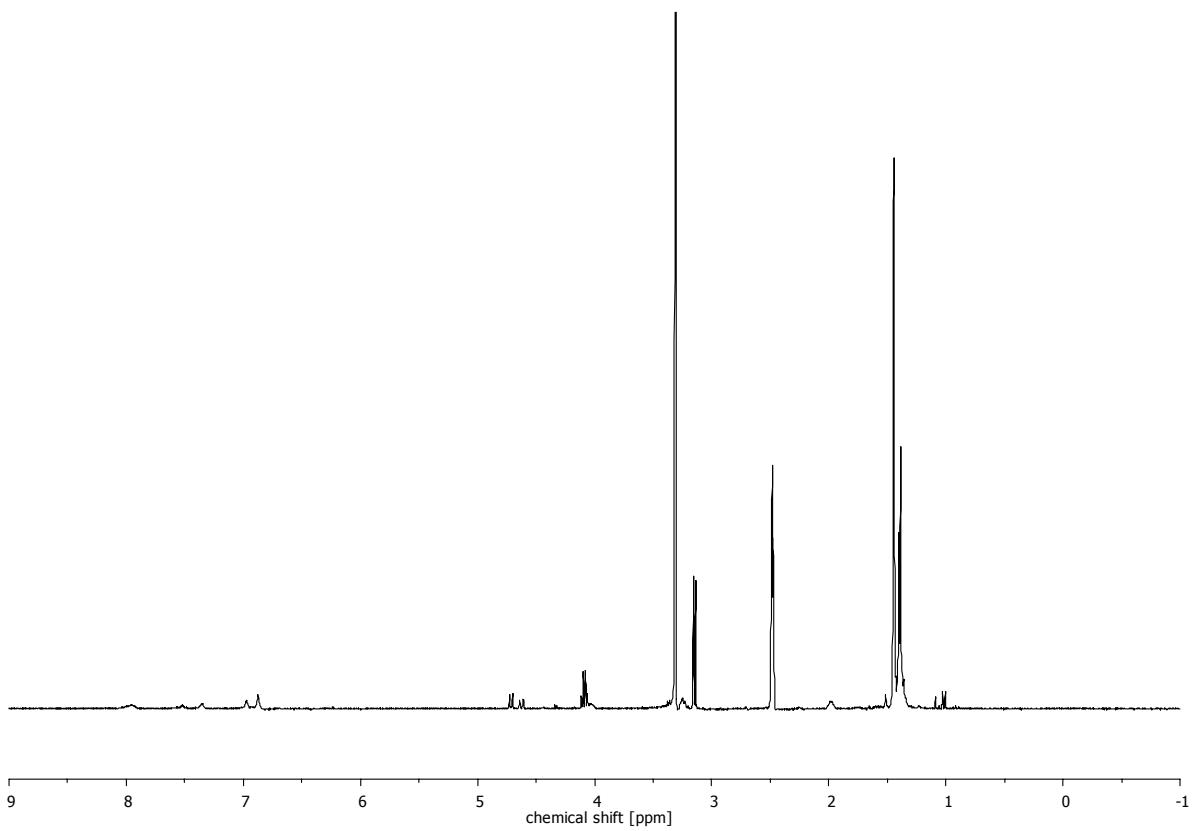
^{1}H NMR spectrum of the mixture of (*rac*)-**17** and (*rac*)-**18** (300 MHz, DMSO-d$_6$)
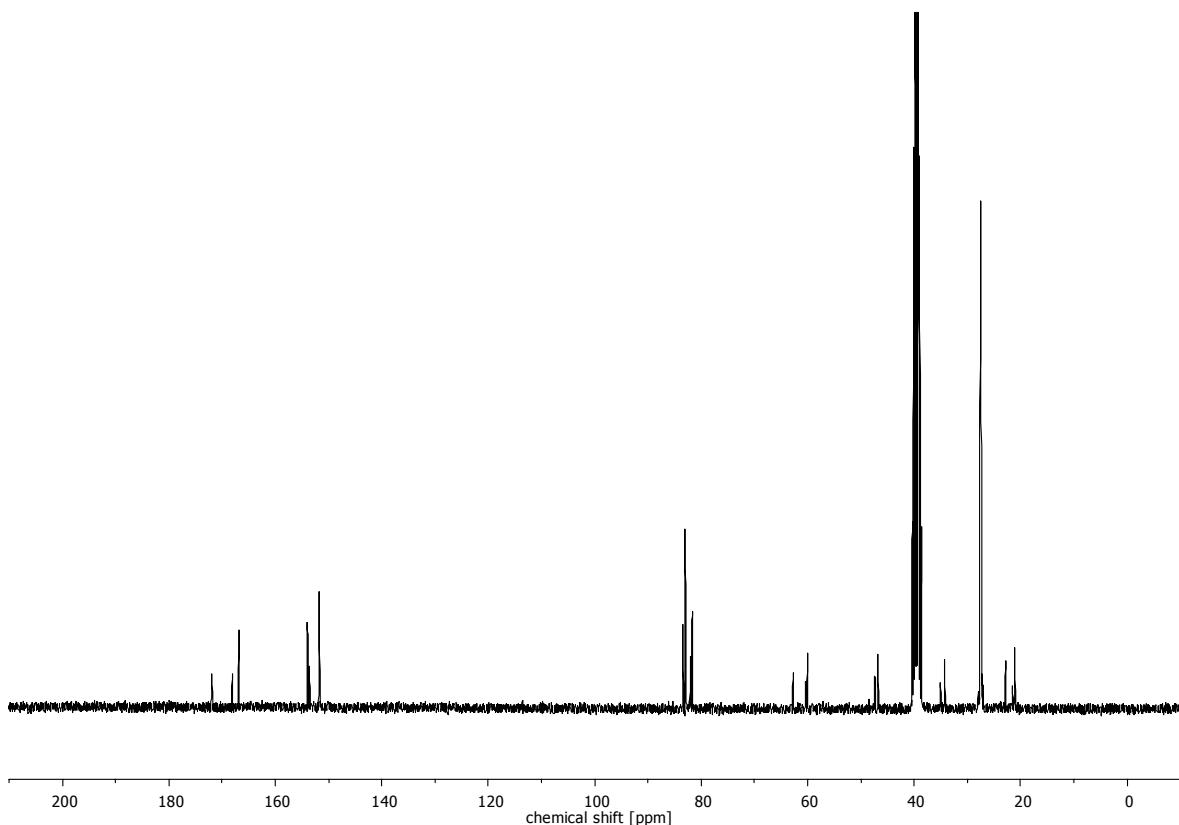
^{13}C NMR spectrum of the mixture of (*rac*)-**17** and (*rac*)-**18** (76 MHz, DMSO-d$_6$)
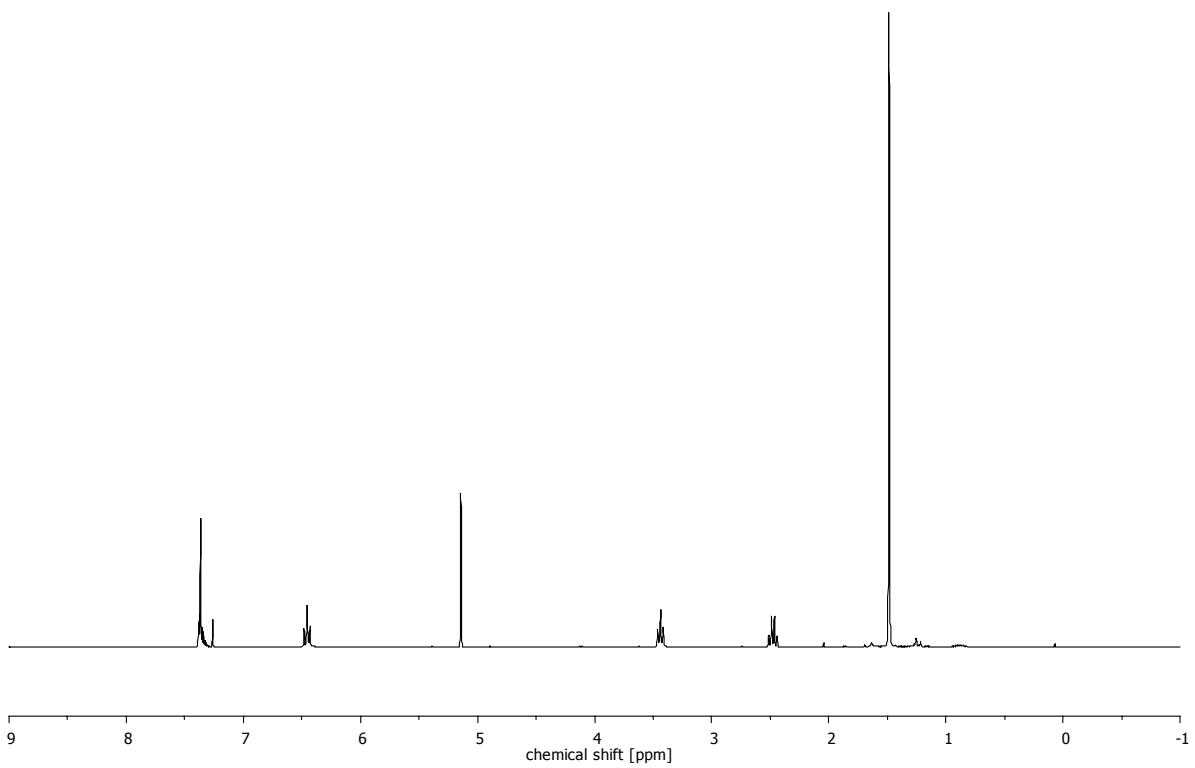
^{1}H NMR spectrum of (*Z*)-**21** (300 MHz, CDCl$_3$)
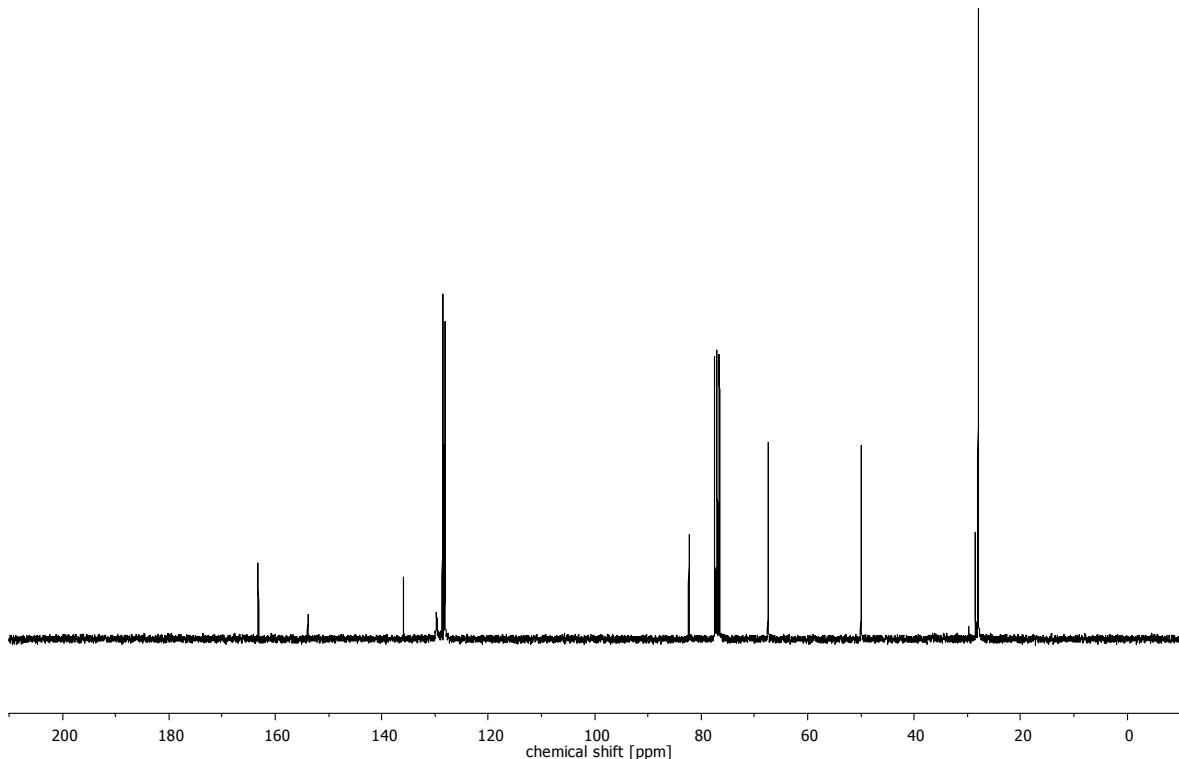
^{13}C NMR spectrum of (*Z*)-**21** (76 MHz, CDCl$_3$)
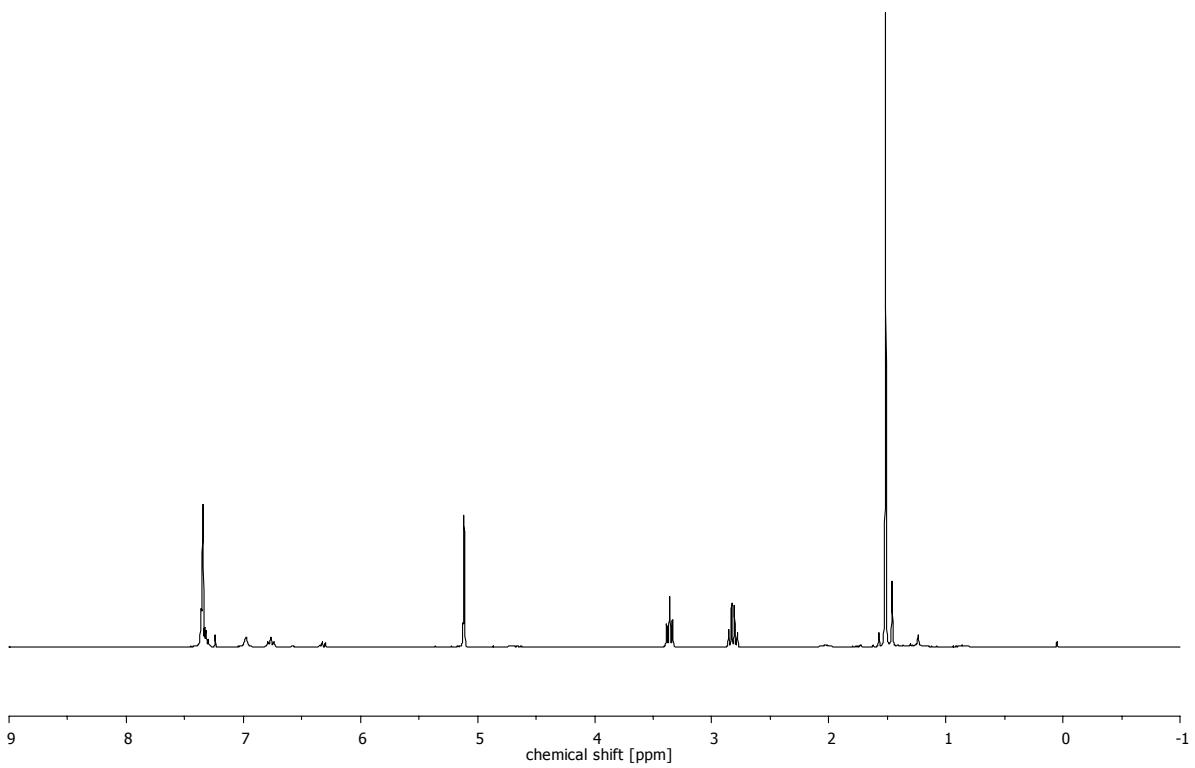
^{1}H NMR spectrum of (*E*)-**21** (300 MHz, CDCl$_3$)
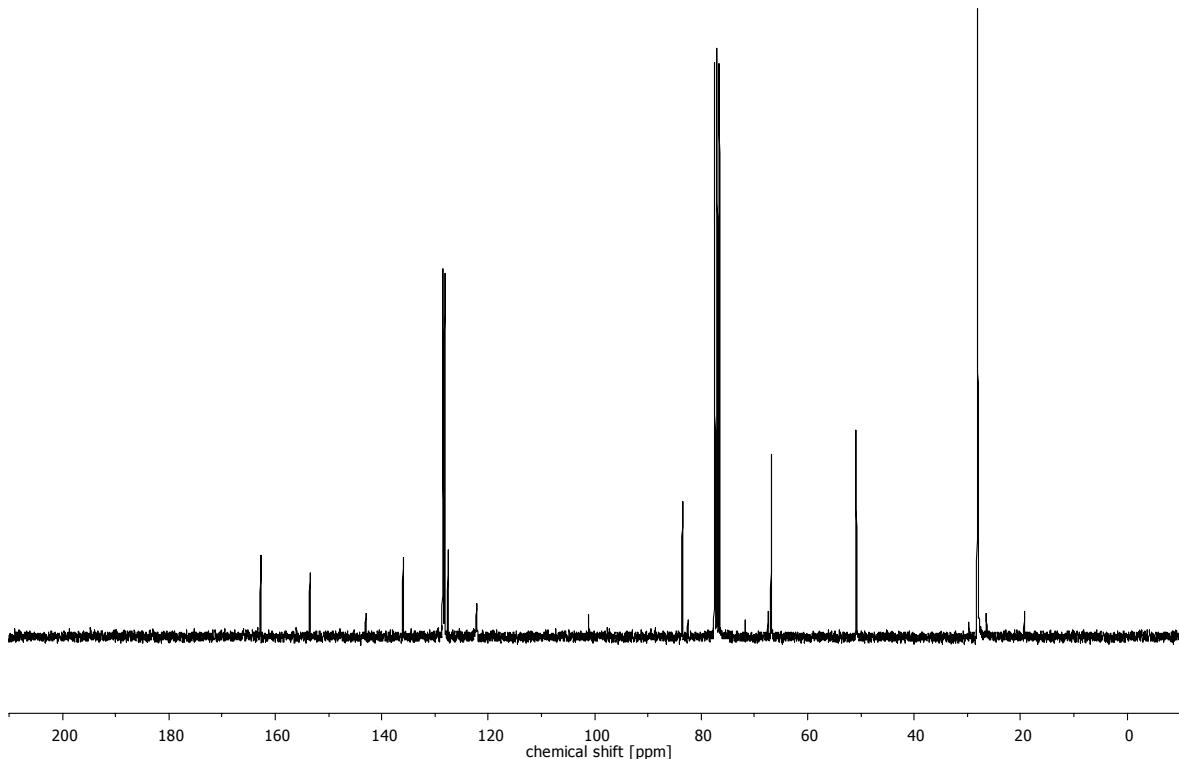
^{13}C NMR spectrum of (*E*)-**21** (76 MHz, CDCl$_3$)
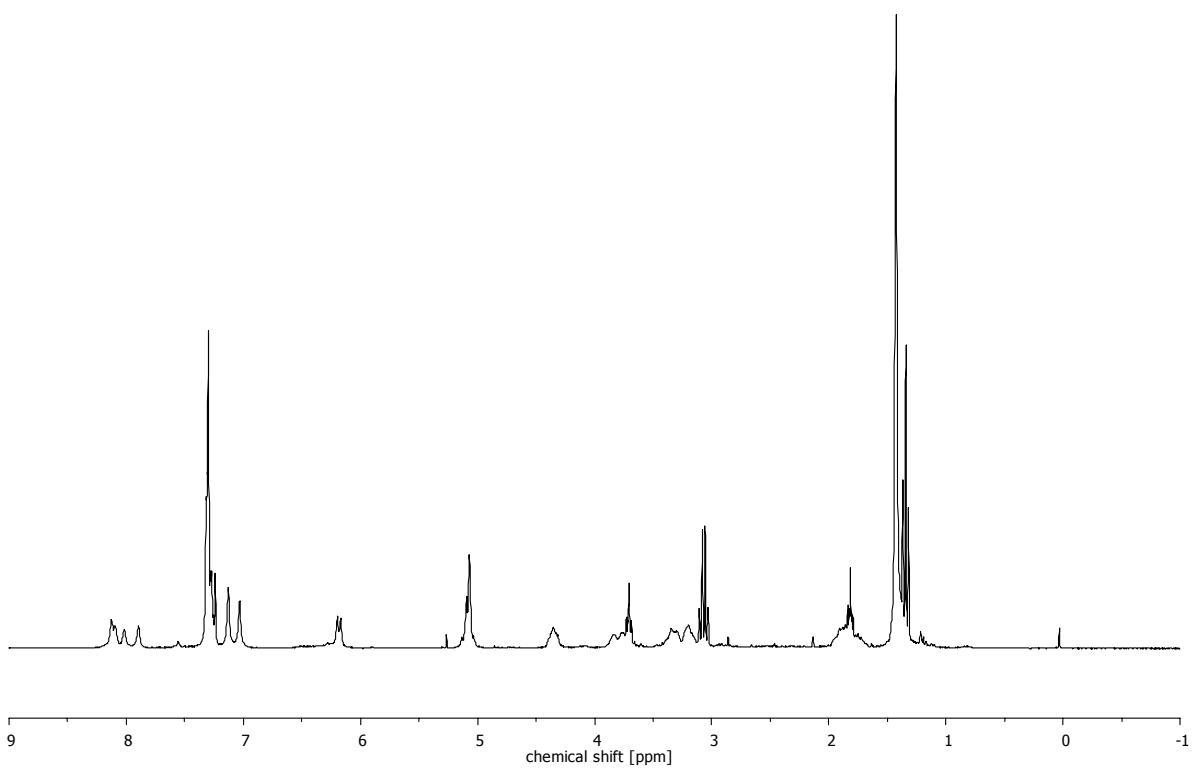
^{1}H NMR spectrum of the mixture of (*rac*)-**23** and (*rac*)-**24** (300 MHz, CDCl$_3$)
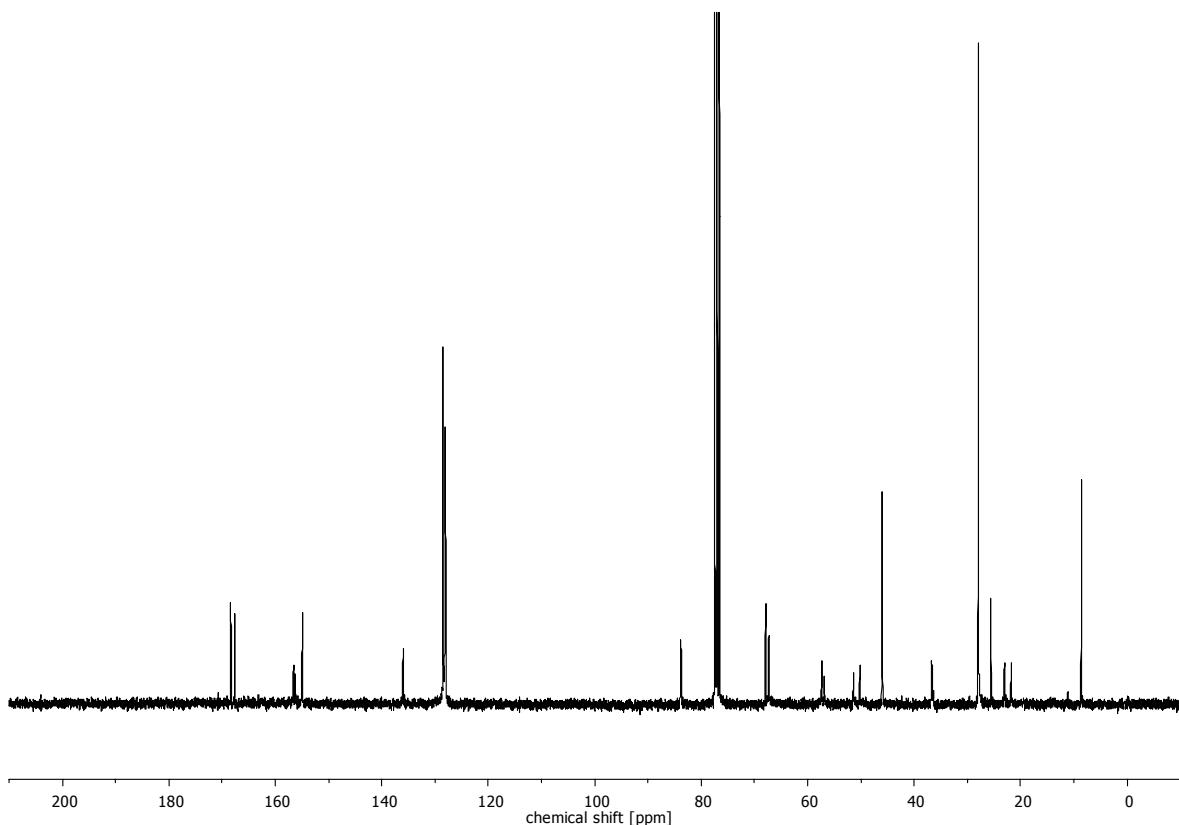
^{13}C NMR spectrum of the mixture of (*rac*)-**23** and (*rac*)-**24** (76 MHz, CDCl$_3$)
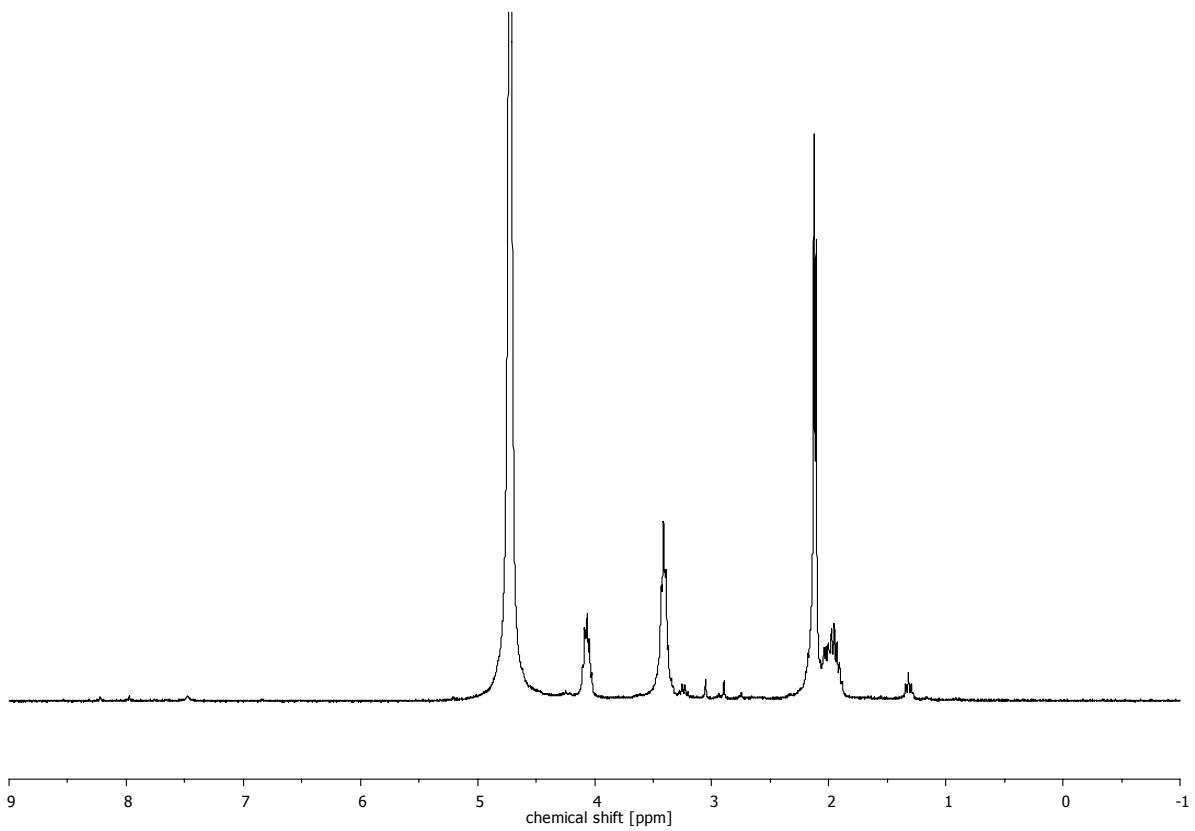
^{1}H NMR spectrum of the mixture of (*rac*)-**27** and (*rac*)-**28** (300 MHz, D$_2$O)
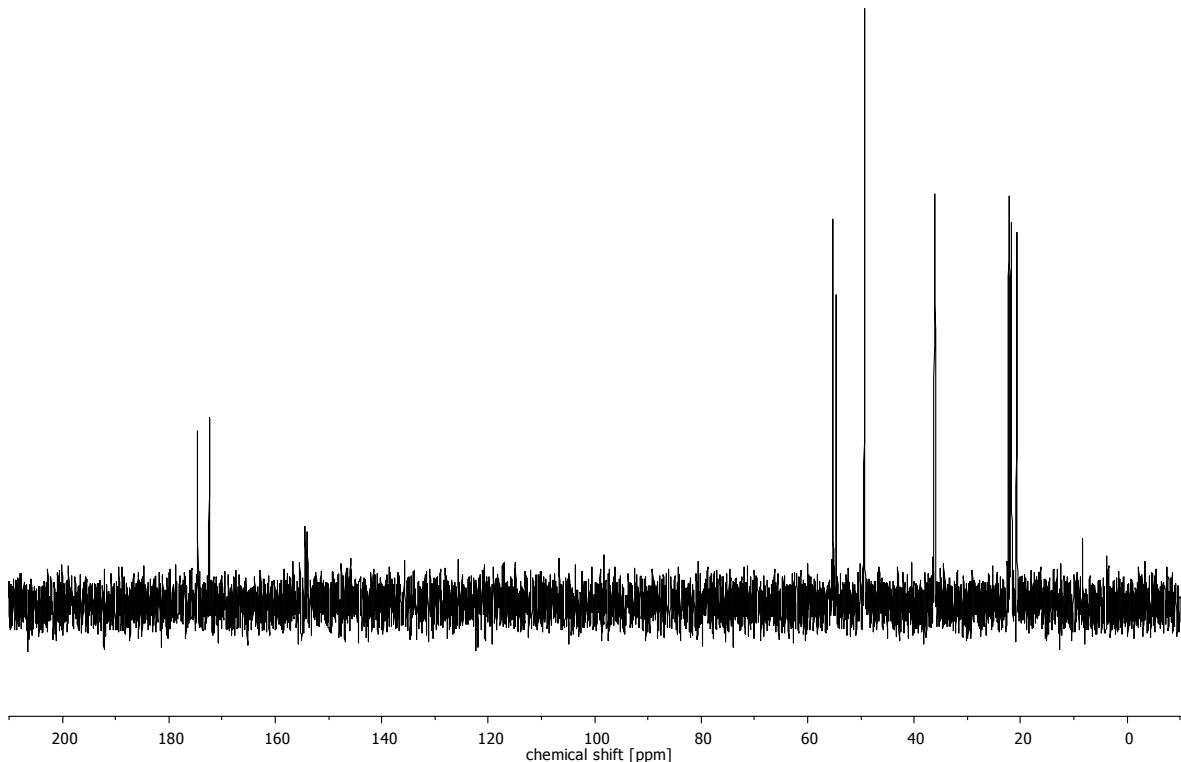
^{13}C NMR spectrum of the mixture of (*rac*)-**27** and (*rac*)-**28** (76 MHz, D$_2$O)

Data on the X-ray crystal structure of (*Z*)-11a
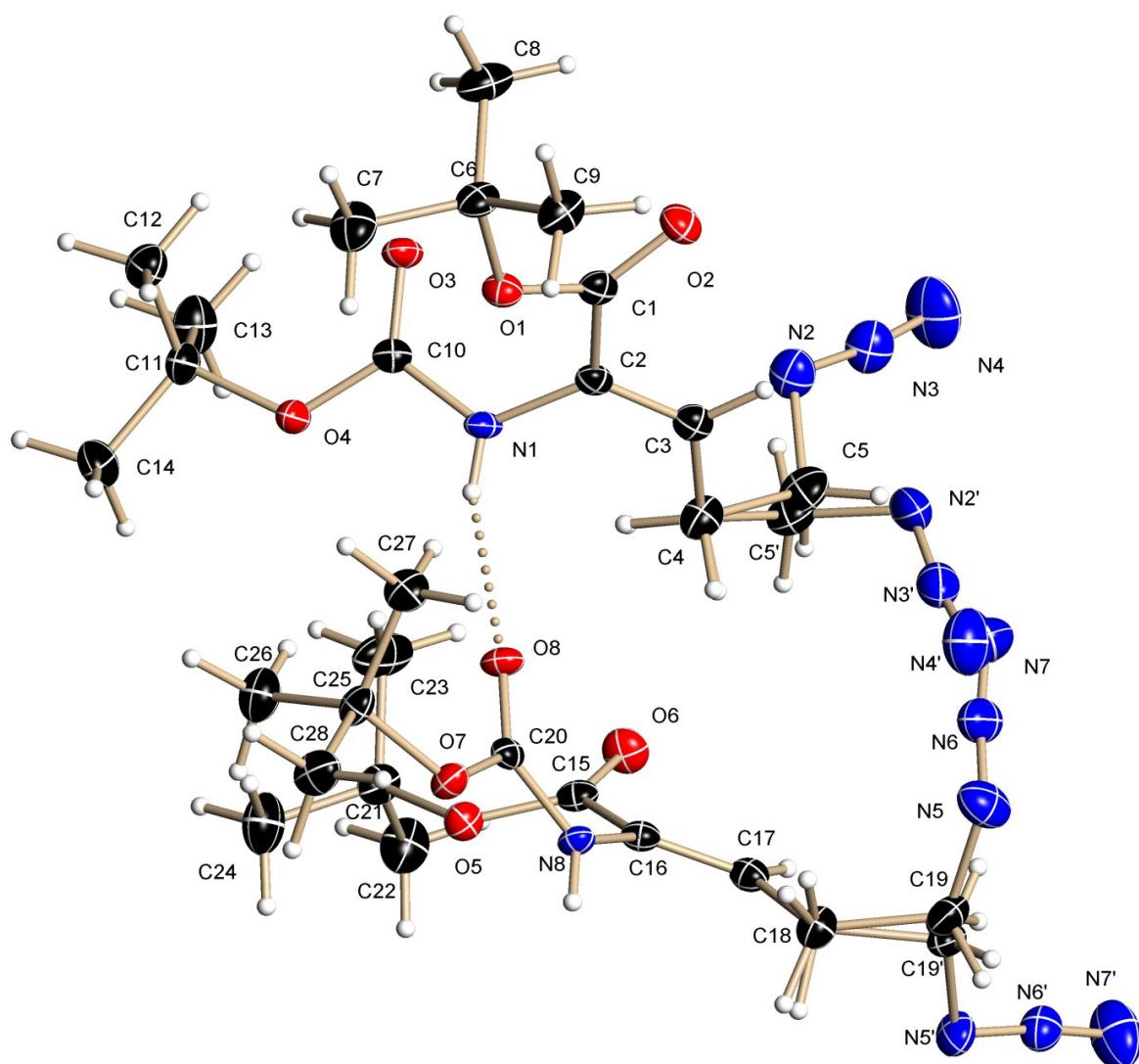
Figure S1. Molecular structure of (Z)-**11** with ellipsoid shown at 50% probability level. Color code: carbon = black, oxygen = red, nitrogen = blue, hydrogen = white.

The crystal of (Z)-**11** was a non-merohedral twin and the two domains were separated using RLATT. The fractional distribution of the second domain refines to 0.4669 (9).

The disorder of the azide groups could be described as a switching between two positions (e.g. N2-N3-N4 to N2'-N3'-N4' and N6-N7-N8 to N6'-N7'-N8' and vice versa). The two position were found in the density difference map and refined using bond lengths restraints and anisotropic displacement parameter restraints. The position of the hydrogen atoms H1 and

H8 were found in the density difference map and refined using bond lengths similarity restraints.

Table S1. Crystallographic data for the structural analysis of (*Z*)-**11a**

Identification code	CCDC 867825
Empirical formula	$C_{14}H_{24}N_4O_4$
Formula weight	312.37
Temperature	100(2) K
Wavelength	71.073 pm
Crystal system	Monoclinic
Space group	$P\,2_1/c$
Unit cell dimensions	a = 1634.8(3) pm α= 90°
	b = 1001.7(2) pm β= 109.24(2)°
	c = 2223.5(3) pm γ = 90°
Volume	$3.4378(10)\ nm^3$
Z	8
Density (calculated)	$1.207\ Mg/m^3$
Absorption coefficient	$0.089\ mm^{-1}$
F(000)	1344
Crystal size	0.15 x 0.10 x 0.08 mm
Theta range for data collection	1.32 to 25.06°.
Index ranges	-19<=h<=18, 0<=k<=11, 0<=l<=26
Reflections collected	61887
Independent reflections	6073 [R(int) = 0.0759]
Completeness to theta = 25.06°	99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9705 and 0.8145
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6073 / 201 / 492
Goodness-of-fit on F^2	1.068
Final R indices [I>2sigma(I)]	R1 = 0.0415, wR2 = 0.0851
R indices (all data)	R1 = 0.0575, wR2 = 0.0911
Extinction coefficient	0.0019(3)
Largest diff. peak and hole	0.192 and -0.185 e.Å^{-3}